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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/688,851	10/16/2000	Jeffrey M. Staub	15868/02	1808

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EXAMINER	
HELMER, GEORGIA L	
ART UNIT	PAPER NUMBER
1638	18

DATE MAILED: 06/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/688,851	Applicant(s) STAUB ET AL.	
	Examiner Georgia L. Helmer	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2000 and 18 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-23 and 33-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *17* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Restriction election

1. The Office acknowledges the receipt of Applicant's restriction election, Amendment Paper No. 16, filed 4/18/02. Applicant elects Group V, claims 24-32 with traverse, stating that it would not create an undue burden on Examiner to search all the claims. Applicant's traversal is unpersuasive for the following reasons: a search of all the inventions would be overlapping but not coextensive, and would create an undue burden. Claims 1-35 are pending. Claims 1-23 and 33-35 are nonelected. Claims 24-32 are examined in the instant application. This restriction is made FINAL.

Specification

Sequence Listing

2. Applicant's CRF and paper sequence listing have been entered.

Information Disclosure Statement

3. An initialed and dated copy of Applicant's IDS form 1449, Paper No. 17, is attached to the instant Office action.

Claim Rejections - 35 USC § 112-second

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 24-32 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 24

- "retransforming" implies the cell plastid is already transformed;
- "a first recombinant DNA sequence" implies a second such sequence, but the second is never mentioned;
- "plastid construct" is unclear; is this a plastid constructed of something, or is it a construct to be introduced into a plastid?
- "said plant cells" (lines 10) lacks antecedent basis ;
- "said first DNA construct" lacks antecedent basis ;
- "a second construct" implies a first construct, and none is recited;
- "said plants" (line 13) lacks antecedent basis ;
- is an incomplete method claim, because the desired product is not produced in the final step of the method.
- Furthermore, for the method to function to retransform a plant cell plastid, the second construct introduced needs to be a plastid construct.

In claim 25,

- "a third recombinant" is unclear—a recombinant what? This is further unclear because a third recombinant implies a second recombinant, and there is none.

- Lines 18 and 19 need to recite some functional linkage between the three mentioned elements.

In claim 26,

- It is unclear where a "first DNA sequence" and a "second DNA sequence" are positioned relative to each other.
- It is further unclear how these two sequences are physically linked.

In claim 27, "comprises" is suggested in place of "is".

In claim 28,

- the phrase "for example" or "i.e." renders the claim indefinite because it is unclear whether the phrase following "i.e." is intended to be a claim limitation. See MPEP § 2173.05(d).

In claim 29, "excision" lacks antecedent basis.

- "whereby the DNA sequence between the said first and said second recombining sites is excised" is suggested as alternative language.

In claim 32, "are" should be changed to "is".

Correction and/or clarification are required.

Claim Rejections - 35 USC § 112-1st, enablement

5. Claims 24-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

- Enablement is considered in view of the *Wands* factors (MPEP 2164.01(a)). The enablement issues are: *the method of retransforming a plant cell plastid,* the *recombining sites*, and "*an organelle targeting region".*

Re *the method of retransforming a plant cell plastid:* Applicant claims (Claim 24) a method for retransforming a plant cell plastid comprising

i) introducing into a plant cell a first recombinant DNA sequence comprising a plastid construct comprising at least one DNA sequence, and at least two recombining sites,

ii) providing a recombinase to said plant cells,

iii) regenerating a plant having at least one plant cell containing said first DNA construct, and

iv) introducing a second construct into said plants obtained from said regenerated plant.

As a method for retransforming plastids, the DNA construct ("a second construct") being introduced into the cells having transformed plastids must be delivered to those specific cells having the transformed plastids. Only when the incoming DNA is in the same cell with those plastids, does that incoming DNA physically have the opportunity to retransform the plastids. See Birch, R.G. Annu Rev. Plant Physiol. Plant Mol. Biol. 1997, 48:297-326. Especially p 302 and Figures 1 & 2. The problem here is that the resident transformed plastid and the incoming retransforming DNA have to be in the same cell. No mechanism exists for bringing the two DNA sequences together

otherwise. The claimed invention recites that a plant, having at least one plant cell containing the first DNA sequence, is regenerated, and a second construct is introduced into this regenerated plant. The desired cell could be one cell out of a million cells in the plant.

The state of the art is that DNA can be readily introduced into plant cells and incorporated into the genome of the plant. However DNA is not incorporated into plant cells unless it is introduced into the cell by some means, either biological or mechanical. *No guidance* is given for transforming plant cells in the absence of biologically or mechanically introducing the DNA. It is unpredictable that DNA introduced into a plant having 1,000,000 nontransformed cells and one transformed cell, will be introduced into the one cell already transformed. Without other guidance, one of ordinary skill in the art would have to test many ways of getting the incoming DNA to the single transformed cell and this would require undue experimentation.

Examples. Example 3 is a prophetic example of an in-vivo excision of an antibiotic resistance gene flanked by direct repeats of lox in the presence of Cre recombinase. Example 4 shows tobacco cells having transformed chloroplasts containing a GFP gene disrupted with an antibiotic resistance marker flanked by direct repeat of lox sites. Upon nuclear transformation of these cells with a construct for expressing a chloroplast transit peptide fused 5' to a Cre protein, and expression of the construct, these cells showed functional GFP expression. This demonstrates that a recombinase could be provided to the plastid and function appropriately to excise the

disrupting DNA. However there is no teaching of plastid retransformation, which is the claimed invention.

The breadth of the claims encompass any plant cell and any plastid, any of three recombinase systems-Cre, FLP and R, any organelle-targeting region, any transcription initiation region, and any selectable marker.

Re *the recombining sites*. Claim 32 is to the method of claim 24 wherein each of said recombining sites is selected from the group consisting of Lox, FRT and R. This encompasses a number of combinations, including Lox/Lox, Lox/FRT, FRT/FRT, FRT/R, Lox/R, and R/R. And the sites can be wild-type or mutant. The only way the invention can work to excise intervening DNA is for (a) the recombining sites to be identical sites, and (b) for the identical sites to be positioned in parallel, as direct repeats, flanking the DNA to be excised (Odell et al; 1994. In J Paszkowski, ed, Homologous Recombination in Plants. Kluewer Academic Publishers, Dordrecht, The Netherlands, pps 219-270. See p225 and 239). The specificity of the recombination event is conferred by the recombinase enzyme, which is specific of its cognate recombining site. The prior art does not show, and Applicant does not teach, how to excise DNA flanked by recombining sites, when such sites are combinations other than lox/lox, Frt/Frt, and R/R. It is unpredictable that combinations of sites other than lox/lox, Frt/Frt, and R/R would work; in fact the state of the art teaches that other such combinations are predicted *not* to work.

Re *an organelle targeting region*", recited in claim 25.

The "organelle targeting region" is recited as the means of introducing the recombinase into the plant cell having the transformed plastids. For the system to work in this way, the "organelle targeting region" must be a "plastid targeting region" and the plastid must be the same plastid as recited in claim 24. The invention will not work otherwise. The state of the art is that organelle targeting regions are polypeptide sequences which function to transfer a 3' fused polypeptide to the organelle. The way this works is that the transit sequences are specific of the organelle; chloroplast transit peptides take the 3' fused polypeptide only to chloroplasts. It is unpredictable that a transit sequence for any organelle other than a chloroplast would function appropriately to transfer the polypeptide to the chloroplast. Rather, such a transit sequence would *not* be predicted to function as desired.

In view of the breadth of the claims (any plant cell and any plastid, any of three recombinase systems-Cre, FLP and R, any organelle-targeting region, any transcription initiation region, and any selectable marker), the lack of guidance in the specification, the lack of working examples, undue experimentation would be required to enable the invention as commensurate in scope with the claims.

REMARKS

6. No claims are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 703-308-7023. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Georgia L. Helmer
Patent Examiner
Art Unit 1638
May 31, 2002

PHUONG T. BUI
PRIMARY EXAMINER